WE CLAIM

1. An isolated polypeptide or a derivative or homolog thereof which *in situ* forms part of the extracellular matrix (ECM) in an animal, wherein said polypeptide comprises a von Willebrand Factor A (VA)-related domain encoded by a nucleotide sequence selected from the group consisting of:

(i) a nucleotide sequence substantially as set forth in SEQ ID NO:1;

(ii) a nucleotide sequence substantially as set forth in SEQ ID NO:7;

(iii) a nucleotide sequence having at least about 65% similarity to SEQ ID NO:1; and

(iv) a nucleotide sequence capable of hybridizing to SEQ ID NO:1 or SEQ ID NO:7 or the complement of SEQ ID NO:1 or SEQ ID NO:7 forms under low stringency conditions.

2. The isolated polypeptide of Claim 1, wherein the nucleotide sequence is SEQ ID NO:1.

3. The isolated polypeptide of Claim 1, wherein the nucleotide sequence is SEQ ID NO:7.

4. The isolated polypeptide of Claim 1, wherein the polypeptide is a von Willebrand Factor A-Related Protein (WARP) encoded by the nucleotide sequence selected from the group consisting of:

(i) a nucleotide sequence substantially as set forth in SEQ ID NO:5;

(ii) a nucleotide sequence substantially as set forth in SEQ ID NO:3;

(iii) a nucleotide sequence having at least about 65% similarity to SEQ ID

NO:5; and

(iv) a nucleotide sequence capable of hybridizing to SEQ ID NO:5 or SEQ ID NO:3 or the complement of SEQ ID NO:5 or SEQ ID NO:3 under low stringency conditions.

5. The isolated polypeptide of Claim 4, wherein the polypeptide is encoded by SEQ ID NO:5.

6. The isolated polypeptide of Claim 4, wherein the polypeptide is encoded by SEQ ID NO:3.

7. The isolated polypeptide of Claim 1 comprising an amino acid sequence substantially a set forth in SEQ ID NO:2 or an amino acid sequnce having at least about 65% similarity to SEQ ID NO:2.

8. The isolated polypeptide of Claim 7, wherein the polypepetide comprises the amino acid sequence set forth in SEQ ID NO:2.

9. The isolated polypeptide of Claim 1, comprising an amino acid sequence substantially a set forth in SEQ ID NO:8 or an amino acid sequnce having at least about 65% similarity to SEQ ID NO:8.

10. The isolated polypeptide of Claim 9, comprising an amino acid sequence set forth in SEQ ID NO:8.

11. The isolated polypeptide of Claim 1, comprising an amino acid sequence substantially a set forth in SEQ ID NO:6 or an amino acid sequnce having at least about 65% similarity to SEQ ID NO:6.

12. The isolated polypeptide of Claim 11, comprising an amino acid sequence set forth in SEQ ID NO:6.

13. The isolated polypeptide of Claim 1, comprising an amino acid sequence substantially a set forth in SEQ ID NO:4 or an amino acid sequnce having at least about 65% similarity thereto.

14. The isolated polypeptide of Claim 13, comprising an amino acid sequence set forth in SEQ ID NO:4.

15. An isolated nucleic acid molecule or a derivative or homolog thereof comprising a sequence of nucleotides encoding or complementary to a sequence encoding a polypeptide which *in situ* forms part of the ECM in an animal, wherein said nucleotide sequence is selected from the group consisting of:

(i) a nucleotide sequence substantially set forth in SEQ ID NO:1;

(ii) a nucleotide sequence substantially set forth in SEQ ID NO:7;

(iii) a nucleotide sequence having at least about 65% similarity to SEQ ID NO:1 or SEQ ID NO:7; and

(iv) a nucleotide sequence capable of hybridizing to SEQ ID NO:1 or SEQ ID NO:1 or the complement of SEQ ID NO:1 or SEQ ID NO:7 under low stringency conditions.

16. The isolated nucleic acid molecule of Claim 15, comprising the nucleotide sequence of SEQ ID NO:1.

17. The isolated nucleic acid molecule of Claim 15, comprising the nucleotide sequence of SEQ ID NO:7.

18. The isolated nucleic acid molecule of Claim 15, comprising a nucleotide sequence selected from the group consisting of:

(i) a nucleotide sequence substantially as set forth in SEQ ID NO:5;

(ii) a nucleotide sequence substantially as set forth in SEQ ID NO:3;

(iii) a nucleotide sequence having at least 65% similarity to SEQ ID NO:5 or SEQ ID NO:3; and

(iv) a nucleotide sequence capable of hybridizing to SEQ ID NO:5 or SEQ ID NO:3 or the complement of SEQ ID NO:5 or SEQ ID NO:3 under low stringency conditions.

19. The isolated nucleic acid molecule of Claim 18, comprising the nucleotide sequence of SEQ ID NO:5.

20. The isolated nucleic acid molecule of Claim 18, comprising the nucleotide sequence of SEQ ID NO:3.

21. The isolated nucleic acid molecule of Claim 15, wherein the nucleotide sequence is a cDNA.

22. The isolated nucleic acid molecule of Claim 15, wherein the nucleotide sequence is a genomic sequence.

23. The isolated nucleic acid molecule of Claim 22, wherein the nucleotide sequence is SEQ ID NO:19.

24. A method of producing a recombinant WARP polypeptide, said method comprising

introducing a nucleic acid molecule into a cell,

wherein said nucleic acid comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:5, the complement of SEQ ID NO:3, the complement of SEQ ID NO:5, a nucleotide sequence having at least about 65% similarity to SEQ ID NO:3 or SEQ ID NO:5, the complement of a nucleotide sequence having at least about 65% similarity to

SEQ ID NO:3 or SEQ ID NO:5 of forms or a nucleotide sequence capable of hybridizing to SEQ ID NO:3 or SEQ ID NO:5 under low stringency conditions,

culturing the cell under conditions sufficient to permit expression of said nucleic acid molecule and

recovering the recombinant WARP polypeptide.

25. A method for identifying a nucleotide sequence likely to encode a WARP, said method comprising

interrogating an animal genome database conceptually translated into different reading frames with an amino acid sequence defining a VA domain and

identifying a nucleotide sequence corresponding to a sequence encoding said VA domain.

26. The method of Claim 25, wherein the genome is conceptually translated into from about 3 to about 6 reading frames.

27. The method of Claim 26, wherein the genome is conceptually translated into 6 reading frames.

28. A method of detecting a loss of ECM integrity in an animal, said method comprising screening body fluid from said animal for the presence of a WARP or fragment thereof, wherein the presence of said WARP or fragment is indicative of a loss of ECM integrity.

29. A method for monitoring repair, regeneration or other disease processes in an animal subject, said method comprising screening body fluid from said animal for the presence of a WARP or fragment thereof, wherein the presence of said WARP or a particular level of WARP compared to normal controls is indicative of cartilage cell differentiation and/or a disease condition.

30. A method for detecting a disease condition or a propensity for the development of a disease condition in an animal subject, said method comprising screening body fluid from said animal for a mutation in WARP or in *WARP,* wherein the presence of said mutation is indicative of a likelihood of a disease condition development or a likelihood of the presence of a disease condition.

31. An isolated antibody specific for a polypeptide encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, a nucleotide sequence having at least about 65% similarity to SEQ ID NO: 1, a nucleotide sequence having at least about 65% similarity to SEQ ID NO: 3, a nucleotide sequence having at least about 65% similarity to SEQ ID NO: 5, a nucleotide sequence having at least about 65% similarity to SEQ ID NO: 7, a nucleotide sequence capable of hybridizing to SEQ ID NO:1, a nucleotide sequence capable of hybridizing to SEQ ID NO:3, a nucleotide sequence capable of hybridizing to SEQ ID NO:5, a nucleotide sequence capable of hybridizing to SEQ ID NO:7, a nucleotide sequence capable of hybridizing to the complement of SEQ ID NO:1, a nucleotide sequence capable of hybridizing to the complement of SEQ ID NO:3, a nucleotide sequence capable of hybridizing to the complement of SEQ ID NO:5, and a nucleotide sequence capable of hybridizing to the complement of SEQ ID NO:7.

32. The isolated antibody of Claim 31, wherein the antibody is a monoclonal antibody.

33. The isolated antibody of Claim 31, wherein the antibody is a polyclonal antibody.

34. An isolated antibody specific for a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, and SEQ ID NO:8

35. The isolated antibody of Claim 34, wherein the antibody is a monoclonal antibody.

36. The isolated antibody of Claim 34, wherein the antibody is a monoclonal antibody.

37. A genetically modified animal comprising a modification to a gene encoding a WARP polypeptide.

38. The genetically modified animal of Claim 34, wherein the animal overexpresses a nucleotide sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, a nucleotide sequence having at least about 65% similarity to SEQ ID NO: 1, a nucleotide sequence having at least about 65% similarity to SEQ ID NO: 3, a nucleotide sequence having at least about 65% similarity to SEQ ID NO: 5, a nucleotide sequence having at least about 65% similarity to SEQ ID NO: 7, a nucleotide sequence capable of hybridizing to SEQ ID NO:1, a nucleotide sequence capable of hybridizing to SEQ ID NO:3, a nucleotide sequence capable of hybridizing to SEQ ID NO:5, a nucleotide sequence capable of hybridizing to SEQ ID NO:7, a nucleotide sequence capable of hybridizing to the complement of SEQ ID NO:1, a nucleotide sequence capable of hybridizing to the complement of SEQ ID NO:3, a nucleotide sequence capable of hybridizing to the complement of SEQ ID NO:5, and a nucleotide sequence capable of hybridizing to the complement of SEQ ID NO:7.

39. The genetically modified animal of Claim 34 wherein the animal lacks a functional expression of a gene comprising a nucleotide sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, a nucleotide sequence having at least about 65% similarity to SEQ ID NO: 1, a nucleotide sequence having at least about 65% similarity to SEQ ID NO: 3, a nucleotide sequence having at least about 65%

similarity to SEQ ID NO: 5, a nucleotide sequence having at least about 65% similarity to SEQ ID NO: 7, a nucleotide sequence capable of hybridizing to SEQ ID NO:1, a nucleotide sequence capable of hybridizing to SEQ ID NO:3, a nucleotide sequence capable of hybridizing to SEQ ID NO:5, a nucleotide sequence capable of hybridizing to SEQ ID NO:7, a nucleotide sequence capable of hybridizing to the complement of SEQ ID NO:1, a nucleotide sequence capable of hybridizing to the complement of SEQ ID NO:3, a nucleotide sequence capable of hybridizing to the complement of SEQ ID NO:5, and a nucleotide sequence capable of hybridizing to the complement of SEQ ID NO:7.

40. A target vector for inactivating a gene encoding WARP comprising two segments of genetic material encoding said WARP flanking a positive selectable marker,

wherein said targeting vector inactivates the gene encoding WARP by homologous recombination when said targeting vector is transfected into embryonic stem (ES) cells.

41. The targeting vector of Claim 40, wherein the ES cells derived from from mice, rats, guinea pigs, pigs, sheep or goats.

42. The targeting vector of Claim 41, wherein the ES cells are from mice.